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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/816,989	03/23/2001	Alexander Gad	60807-A-PCT-US/JPW/GJG	7587

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EXAMINER
HUYNH, PHUONG N

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1644	

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14

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/816,989	Applicant(s) GAD ET AL.	
	Examiner " Neon" Phuong Huynh	Art Unit 1644	

-- The MAILING DATE of this communication app ars on th cover sheet with the correspondenc address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *Three* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 March 2001 and 06 August 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *123-143* is/are pending in the application.

4a) Of the above claim(s) *143* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *123-142* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *11-13* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. Claims 123-143 are pending.

2. Applicant's election with traverse of Group II, Claims 70-91 and 94-103 (now claims 123-142) drawn to a method for treating an autoimmune disease that read on the species of multiple sclerosis comprising administering a polypeptide having the amino acid sequence set forth in SEQ ID NO: 1, filed 8/6/02, is acknowledged. The traversal is on the grounds that (1) new claims 123-143 should not be subject to restriction because it would not be an undue burden to examine the prior regarding the use of these 7 specific sequences since the same Examiner has already conducted a prior art search for the same 7 sequences in USNN 09/405,743 and found the seven sequences allowable, (2) the specification on page 37-38 discloses the purified polypeptide are tested in an EAE system which is an animal model of autoimmune disease (Exhibit B), it should be accepted as such that all autoimmune diseases should be examined in this application, (3) If the Examiner applies the election of species requirement to the new claims, and after examining finds the elected species allowable, the Examiner should proceed to examine the other species pursuant to MPEP §809.02(c). (4) Applicant asserts that claim 143, drawn to a method of determining the molecular weight of glatiramer acetate, should be examined in this application because it should not be an undue burden on the Examiner since the seven specific sequences have been allowed. Upon reconsideration, the species requirement of the polypeptide has been extended to SEQ ID NO: 2-7, and the species requirement for autoimmune disease has been extended to such as the ones recited in claims 134-142. However, Claim 143 (Group III) is drawn to a method of determining the molecular weight of glatiramer acetate, which is drawn to a different class and subclass. A search of the method of treating autoimmune disease using the polypeptide selected from the group consisting of SEQ ID NO: 1-7 would not encompass the method of determining molecule weight. It is a burden to search more than one invention. Therefore, the requirement of Group II (now claims 123-142) and Group III is still deemed proper and is therefore made FINAL.

3. Claim 143 is withdrawn from further consideration by the examiner, 37 C.F.R. 1.142(b) as being drawn to non-elected invention.

4. Claims 123-142 are being acted upon in this Office Action.

5. The drawings, filed 3/23/01, are not approved. Please see enclosed PTO 948, Notice of Draftsperson's Patent Drawing Review. Appropriate action is required.

6. The disclosure is objected to because of the following informality: "This application is a continuation of PCT International Application No. PCT/US99/22402...incorporated by reference into the present application" filed by preliminary amendment A on page 1 after the title should be deleted because it is redundant in the subsequent paragraph that discloses "The present application claims the benefited of US Provisional Application... incorporated by reference into the present application" under the heading Related Application as amended by amendment B filed 8/6/02. Appropriate action is required.

7. The references on PTO 1449, filed 8/26/02, 9/16/02, and 10/23/02 have been crossed out because none of the references have been submitted to the Office.

8. Claim 134 is objected to because "rheumatoid arthritis" is recited twice.

9. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. Claims 123-142 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling only for a method for treating an autoimmune disease wherein the autoimmune disease is multiple sclerosis in a mammal comprising administering the mammal a purified polypeptide comprising the amino acid sequence of SEQ DI NO: 2 and 7, **does not** reasonably provide enablement for (1) a method of treating or "**preventing**" *any* autoimmune disease in any mammal comprising administering to the mammal a purified polypeptide having the amino acid sequence set forth in SEQ ID NO: 1-7 or a mixture of purified polypeptides; (2) said method wherein the purified polypeptide consists entirely of L-amino acids or D-amino acids; (3) a method of treating or "**preventing**" *any* "**autoimmune disease**" in any mammal comprising administering to the mammal a pharmaceutical composition consisting essentially of

any purified polypeptide having the amino acid sequence set forth in SEQ ID NO: 1-7 or a mixture of purified polypeptides, and a pharmaceutically acceptable carrier; (4) a method of "**preventing**" *any* autoimmune disease such as any B cell mediated autoimmune disease, any T cell mediated autoimmune disease, *any* demyelinating disease, *any* inflammatory disease, any autoimmune disease such as rheumatoid arthritis, osteoarthritis, multiple sclerosis, autoimmune hemolytic anemia, autoimmune oophoritis, autoimmune thyroiditis, autoimmune uveoretinitis, Crohn's disease, chronic immune thrombocytopenic purpura, colitis, contact sensitivity disease, diabetes mellitus, idiopathic myxedema, myasthenia gravis, psoriasis, pemphigus vulgaris, or systemic lupus erythematosus, graft versus host disease (GVHD), host versus graft disease (HVGD) or delayed-type hypersensitivity comprising administering to the mammal a purified polypeptide having the amino acid sequence set forth in SEQ ID NO: 1-7, and (5) a method of "**treating**" *any* autoimmune disease such as any B cell mediated autoimmune disease, any T cell mediated autoimmune disease, any demyelinating disease, any inflammatory disease, rheumatoid arthritis, osteoarthritis, autoimmune hemolytic anemia, autoimmune oophoritis, autoimmune thyroiditis, autoimmune uveoretinitis, Crohn's disease, chronic immune thrombocytopenic purpura, colitis, contact sensitivity disease, diabetes mellitus, idiopathic myxedema, myasthenia gravis, psoriasis, pemphigus vulgaris, or systemic lupus erythematosus, graft versus host disease (GVHD), host versus graft disease (HVGD) or delayed-type hypersensitivity comprising administering to the mammal a purified polypeptide having the amino acid sequence set forth in SEQ ID NO: 1-7. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in **scope** with these claims.

Factors to be considered in determining whether undue experimentation is required to practice the claimed invention are summarized *In re Wands* (858 F2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)). The factors most relevant to this rejection are the scope of the claim, the amount of direction or guidance provided, the lack of sufficient working examples, the unpredictability in the art and the amount of experimentation required to enable one of skill in the art to practice the claimed invention. The specification disclosure is insufficient to enable one skilled in the art to practice the invention as broadly claimed without an undue amount of experimentation.

The specification discloses only a method for treating female (SJL/J x BALB/c) mice with mouse spinal cord homogenate to induce EAE, which is a model for multiple sclerosis and a

polypeptide selected from the group consisting of SEQ ID NO: 2, 4, 5, 6 and 7. The results show in Table 14 that only polypeptides SEQ ID NO: 2, and 7 block the progression of EAE while treatment with polypeptides of SEQ ID NO: 4, 5 and 6 fail to block the progression of EAE (see page 38). In fact, treatment with polypeptides of SEQ ID NO: 4-6 does not prevent EAE because it has a mean onset of EAE at days 11.7, 14, and 12, respectively, as compared to control (11.3 days). The delayed onset of disease for polypeptides of SEQ ID NO: 4 and 6 is not significantly different than the control. Note, the block in the progression of disease is the treatment using polypeptides of SE QIDNO: 2 and 7 could simply due to a delay in the onset of EAE because there is insufficient information on the time course in the specification as filed, much less about relapse.

The specification does not teach a method of "preventing" *any* autoimmune disease mentioned above because of the following reasons:

(1) There is insufficient guidance and in vivo working examples that the claimed method of using any polypeptides mentioned above could "prevent" any autoimmune disease. The term "preventing" as defined in the Webster's II New Riverside University Dictionary on page 933 as "to thwarting or warding off illness or disease". The specification discloses in Table 14 on page 38 that treatment with polypeptides of SEQ ID NO: 4-6 fails to "prevent" EAE, but rather the treatment delays the onset of EAE by 1 to 3 days where the EAE model is for early onset of multiple sclerosis. The EAE model used by Applicant is not appropriate for chronic relapse autoimmune disease, let alone for any other disease such as the ones recited in claim 134. Further, the experiments were not carried out long enough to see the effect of polypeptide of SEQ ID NO: 1 and 7 on chronic relapsing multiple sclerosis. In humans, the claimed autoimmune diseases encompassed by the claimed method are already established before therapy is offered. It is not clear that administering the claimed polypeptides shortly after (48 hours) or simultaneous given mouse spinal cord homogenate to induce acute onset of EAE accurately reflect on the chronic relapsing nature of autoimmune disease.

Van Noort et al teach the type of EAE induced is dependent on the immunization protocol, animal strain, and antigen used and some antigen used resulted in acute episode of EAE, others induce a chronic relapsing disease (See page 169, first full paragraph, in particular). Van Noort et al further teach that it is the chronic relapsing EAE that is reminiscent of multiple sclerosis (MS) because animals develop accumulating neurological features of the induced disease (See page 169. first full paragraph, in particular).

(2) Even if the method is limited to method of treating autoimmune disease by administering polypeptide selected from the group consisting of SEQ ID NO: 2, and 7, it is not clear that reliance on the EAE experimental model, which is a model for acute multiple sclerosis, accurately reflects on other autoimmune disease such as the ones recited in claims 134-142 since the EAE model is irrelevant to other disease such as the ones recited in claim 134-142, much less preventing chronic relapse multiple sclerosis.

Van Noort et al teach experimental allergic encephalomyelitis (EAE) is only a model for multiple sclerosis and the EAE model is not appropriate for other autoimmune diseases such as rheumatoid arthritis, osteoarthritis, autoimmune hemolytic anemia, autoimmune oophoritis, autoimmune thyroiditis, autoimmune uveoretinitis, Crohn's disease, chronic immune thrombocytopenic purpura, colitis, contact sensitivity disease, diabetes mellitus, idiopathic myxedema, myasthenia gravis, psoriasis, pemphigus vulgaris, or systemic lupus erythematosus, graft versus host disease (GVHD), host versus graft disease (HVGD) or delayed-type hypersensitivity (See page 167 bridging page 168, Table III, in particular). Further, there is no guidance and working example demonstrating that any of the polypeptide such as SEQ ID NO: 1-7 could treat, much less could prevent any disease mentioned above.

(3) Even if the method is limited to treating multiple sclerosis, the specification on page 38 discloses that only two (SEQ ID NO: 2 and 7) out of seven polypeptides that could block EAE. However, the method of treating EAE with polypeptides of SEQ ID NO: 4, 5 or 6 delays the onset of disease with varying degree of blocking while polypeptides of SEQ ID NO: 1 and 3 have no in vivo data.

Pender *et al* teach that many therapies that are effective in the animal model such as experimental autoimmune encephalomyelitis (EAE), are either ineffective in MS or in the case of gamma interferon, lenercept and altered peptide ligands actually make multiple sclerosis (MS) worse (See abstract, in particular).

Given the infinite number of autoimmune disease, the limited working example and the unpredictable nature of the polypeptide even for just multiple sclerosis, a person of skill in the art could not predict which particular amino acid sequences of the claimed polypeptides are effective for treating EAE, let alone treating or preventing any autoimmune disease as encompassed by the claimed method.

For these reasons, it would require undue experimentation of one skilled in the art to practice the claimed invention. See page 1338, footnote 7 of Ex parte Aggarwal, 23 USPQ2d 1334 (PTO Bd. Pat App. & Inter. 1992).

In re wands, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988), the decision of the court indicates that the more unpredictable the area is, the more specific enablement is necessary. In view of the quantity of experimentation necessary, the limited working example, the unpredictability of the art, the lack of sufficient guidance in the specification and the breadth of the claims, it would take an undue amount of experimentation for one skilled in the art to practice the claimed invention.

11. Claims 123-142 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention.

The specification does not reasonably provide a **written description** of (1) a method of treating or "**preventing**" *any* autoimmune disease in any mammal comprising administering to the mammal a purified polypeptide having the amino acid sequence set forth in SEQ ID NO: 1-7 or a mixture of purified polypeptides; (2) said method wherein the purified polypeptide consists entirely of L-amino acids or D-amino acids; (3) a method of treating or "**preventing**" *any* "**autoimmune disease**" in any mammal comprising administering to the mammal a pharmaceutical composition consisting essentially of any purified polypeptide having the amino acid sequence set forth in SEQ ID NO: 1-7 or a mixture of purified polypeptides, and a pharmaceutically acceptable carrier; (4) a method of "**preventing**" *any* autoimmune disease such as any B cell mediated autoimmune disease, any T cell mediated autoimmune disease, *any* demyelinating disease, *any* inflammatory disease, any autoimmune disease such as rheumatoid arthritis, osteoarthritis, multiple sclerosis, autoimmune hemolytic anemia, autoimmune oophoritis, autoimmune thyroiditis, autoimmune uveoretinitis, Crohn's disease, chronic immune thrombocytopenic purpura, colitis, contact sensitivity disease, diabetes mellitus, idiopathic myxedema, myasthenia gravis, psoriasis, pemphigus vulgaris, or systemic lupus erythematosus, graft versus host disease (GVHD), host versus graft disease (HVGD) or delayed-type hypersensitivity comprising administering to the mammal a purified polypeptide having the amino acid sequence set forth in SEQ ID NO: 1-7, and (5) a method of "**treating**" *any*

autoimmune disease such as any B cell mediated autoimmune disease, any T cell mediated autoimmune disease, any demyelinating disease, any inflammatory disease, rheumatoid arthritis, osteoarthritis, autoimmune hemolytic anemia, autoimmune oophoritis, autoimmune thyroiditis, autoimmune uveoretinitis, Crohn's disease, chronic immune thrombocytopenic purpura, colitis, contact sensitivity disease, diabetes mellitus, idiopathic myxedema, myasthenia gravis, psoriasis, pemphigus vulgaris, or systemic lupus erythematosus, graft versus host disease (GVHD), host versus graft disease (HVGD) or delayed-type hypersensitivity comprising administering to the mammal a purified polypeptide having the amino acid sequence set forth in SEQ ID NO: 1-7.

The specification discloses only a method for treating female (SJL/J x BALB/c) mice with mouse spinal cord homogenate to induce EAE, which is a model for multiple sclerosis and a polypeptide selected from the group consisting of SEQ ID NO: 2, 4, 5, 6 and 7. The results show in Table 14 that only polypeptides SEQ ID NO: 2, and 7 block the progression of EAE while treatment with polypeptides of SEQ ID NO: 4, 5 and 6 fail to block the progression of EAE (see page 38). In fact, treatment with polypeptides of SEQ ID NO: 4-6 does not prevent EAE because it has a mean onset of EAE at days 11.7, 14, and 12, respectively, as compared to control (11.3 days). The delayed onset of disease for polypeptides of SEQ ID NO: 4 and 6 is not significantly different than the control. Note, the block in the progression of disease is the treatment using polypeptides of SE QIDNO: 2 and 7 could simply due to a delay in the onset of EAE because there is insufficient information on the time course in the specification as filed, much less about relapse.

With the exception of the specific method of treating multiple sclerosis by administering the specific polypeptides mentioned above, there is insufficient written description about the method of *treating* any autoimmune disease such as any B cell mediated autoimmune disease, any T cell mediated autoimmune disease, any demyelinating disease, any inflammatory disease, rheumatoid arthritis, osteoarthritis, autoimmune hemolytic anemia, autoimmune oophoritis, autoimmune thyroiditis, autoimmune uveoretinitis, Crohn's disease, chronic immune thrombocytopenic purpura, colitis, contact sensitivity disease, diabetes mellitus, idiopathic myxedema, myasthenia gravis, psoriasis, pemphigus vulgaris, or systemic lupus erythematosus, graft versus host disease (GVHD), host versus graft disease (HVGD) or delayed-type hypersensitivity comprising administering to the mammal a purified polypeptide having the amino acid sequence set forth in SEQ ID NO: 1-7. Further, there is insufficient written description about the method of "**preventing**" *any* autoimmune disease such as the ones recited in

claims 134-142 comprising administering to the mammal a purified polypeptide having the amino acid sequence set forth in SEQ ID NO: 1-7. Further, there is inadequate written description about the method of treating any autoimmune disease mentioned above comprising administering any polypeptides such as SEQ ID NO: 1 and 3.

The specification discloses only treating multiple sclerosis by administering polypeptides selected from the group consisting of SEQ ID NO: 2, 4, 5, 6 and 7 using the EAE as a model for multiple sclerosis. Given the lack of a written description of *any* additional representative species of autoimmune disease that can be treated or prevented using any polypeptide of SEQ ID NO: 1-7, one of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus, Applicant was not in possession of the claimed genus. *See University of California v. Eli Lilly and Co. 43 USPQ2d 1398.*

Applicant is directed to the Revised Interim Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

12. No claim is allowed.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to "Neon" Phuong Huynh whose telephone number is (703) 308-4844. The examiner can normally be reached Monday through Friday from 9:00 am to 6:00 p.m. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

14. Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform to the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-7401.

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